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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/772,114	01/26/2001	Michael A. Whitney	AURO1120-5	8989

7590

02/28/2003

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EXAMINER
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FREDMAN, JEFFREY NORMAN

ART UNIT	PAPER NUMBER
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1634

DATE MAILED: 02/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/772,114

Applicant(s)

WHITNEY ET AL.

Examiner

Jeffrey Fredman

Art Unit

1637

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 29 March 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 171-184 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 171-184 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

## **DETAILED ACTION**

### ***Election/Restrictions***

1. Applicant's election of Group III, claims 171-184 in Paper No. 8 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

### ***Priority***

2. The current application claims priority to 09/047,862 which is a CIP of 09/021,974 which is a CIP of PCT/US97/17395 which is a CIP of 08/719,697. The examiner has reviewed the specifications of both PCT/US97/17395 and 08/719,697. Neither the PCT nor the 08/719,697 specifications provide descriptive support for the claimed invention. For example, no support for the requirement that the clonal cells exhibit a 1.5 fold change in B-lactamase expression was found in either the PCT or 08/719,697. The priority documents also lack other limitations such as the concept of a "cell sensor panel" itself. Consequently, the current claims are not given priority to the PCT or to 08/719,697.

### ***Claim Rejections - 35 USC § 112***

3. Claims 171-177 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 171 recites the limitation "said target" in line 6. There is insufficient antecedent basis for this limitation in the claim because the word "target" does not

appear prior to the phrase "said target". While the examiner would try to read the claim in context, it is unclear which of the previous elements is intended to be the target, since the target could be the "clonal cells" themselves, the "fusion RNA" inside the cells, the "cellular RNA transcript" or even the "beta lactamase polynucleotide".

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 171-184 are rejected under 35 U.S.C. 103(a) as being unpatentable over Forrester et al (Proc. Natl. Acad. Sci. (February 1996) 93:1677-1682) in view of Tsien et al (WO 96/30540) and further in view of Hicks et al (Meth. Enzymol. (1995) 254:263-275).

Forrester teaches a plurality of clonal cells (see abstract), wherein each clonal cell comprises a distinct fusion RNA of a cellular RNA transcript and a B-galactosidase polynucleotide encoding a B-galactosidase, stating "Integration of PT1-ATG into the intron of an active gene can generate a fusion transcript between lacZ and an endogenous trapped gene" (see page 1677, column 2) and,

Wherein said clonal cells exhibit as much as a 12.4 fold induction in B-galactosidase expression in response to the induction of expression of said target in said clonal cells (See page 1678, table 1) in response to exposure of said clonal cells to a ligand for said target (see page 1677, column 2),

Wherein said clonal cells were selected from a population of cells transfected with the PT1-ATG vector and wherein said vector lacks a promoter to express said B-galactosidase (See page 1677, column 2).

Forrester further teaches clonal cells under the control of the retinoic acid response element (see page 1678, table 1) and teaches the use of 24 well plates (a two dimensional array) (see page 1677, column 2). Forrester teaches screening of 3,600 ES (embryonic stem) cell colonies with 202 positive colonies picked and retested in the 24 well plates (see page 1678, column 1).

Forrester does not teach the use of B-lactamase in the place of B-galactosidase as the reporter. Also, it is unclear whether the vector of Forrester is a viral vector.

Tsien teaches the use of B-lactamase in the place of B-galactosidase (see page 39).

Hicks teaches the use of retroviral gene trap vectors (see page 267, page 268, figure 2 and entire reference).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Forrester to substitute the use the B-lactamase enzyme of Tsien for B-galactosidase since Tsien teaches "[U]se of the novel beta lactamase substrate compounds of the present invention will provide distinct advantages over known reporter genes (including ... beta-galactosidase ...) and their requisite substrates (page 39, lines 16-22)." Tsien identifies advantages of the use of B-lactamase which include high efficiency of the enzyme (see page 39, line 1), since the enzymes are nearly optimally diffusion controlled (see page 10, lines 1-5). Also, the B-lactamase is sensitive and easily detected within living cells (see page 16).


It would further have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Forrester to use retroviral vectors as taught by Hicks since Hicks states that relative to ordinary vectors "[R]etrovirus vectors are easier to use, especially for large scale mutagenesis, and the structure of the recombination products is more predictable (see page 267). An ordinary practitioner would have been motivated to modify the method of Forrester in view of Tsien to use retrovirus gene trap vectors since the method of Forrester is a large scale mutagenesis method screening 3,600 colonies and since Hicks expressly teaches that this would be easier using a retrovirus gene trap vector.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is 703-308-6568. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Jeffrey Fredman  
Primary Examiner  
Art Unit 1637

February 19, 2003